Claims

1. An isolated cell that recombinantly expresses an N-type calcium channel comprising a $Ca_V2.2$ subunit that comprises exon e37a ($Ca_V2.2e[37a]$).

2. The isolated cell of claim 1, wherein the $Ca_V2.2e[37a]$ subunit has a human sequence.

3. The isolated cell of claim 1, wherein the $Ca_V2.2e[37a]$ subunit has a mouse sequence.

4. The isolated cell of claim 1, wherein the $Ca_V2.2e[37a]$ subunit has a rat sequence.

5. The isolated cell of any of claims 1-4, wherein the cell is a neuron.

6. The isolated cell of any of claims 1-4, wherein the cell is an oocyte.

7. An isolated neuron that expresses an N-type calcium channel comprising a $Ca_V2.2$ subunit that comprises exon e37a ($Ca_V2.2e[37a]$).

8. The isolated neuron of claim 7, wherein the neuron further expresses a marker of nociceptive neurons.

9. The isolated neuron of claim 8, wherein the marker of nociceptive neurons is $Na_V1.8$.

10. The isolated neuron of claim 8, wherein the marker of nociceptive neurons is vanilloid receptor VR1.

11. The isolated neuron of claim 8, wherein the neuron expresses both $Na_V1.8$ and vanilloid receptor VR1.

12. A method for identifying lead compounds for a pharmacological agent useful in the treatment of disease associated with increased or decreased voltage regulated calcium influx mediated by a N-type calcium channel containing a $Ca_V2.2e[37a]$ subunit comprising

providing a cell or other membrane-encapsulated space comprising a $Ca_V2.2e[37a]$ polypeptide;

contacting the cell or other membrane-encapsulated space with a candidate pharmacological agent under conditions which, in the absence of the candidate pharmacological agent, cause a first amount of voltage regulated calcium influx into the cell or other membrane-encapsulated space; and

determining a test amount of voltage regulated calcium influx as a measure of the effect of the lead compounds for a pharmacological agent on the voltage regulated calcium influx mediated by a N-type calcium channel containing a $Ca_V2.2e[37a]$ subunit,

wherein a test amount of voltage regulated calcium influx which is less than the first amount indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which reduces voltage regulated calcium influx and wherein a test amount of voltage regulated calcium influx which is greater than the first amount indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which increases voltage regulated calcium influx.

13. The method of claim 12, further comprising the step of loading the cell or other membrane-encapsulated space with a calcium-sensitive compound which is detectable in the presence of calcium, wherein the calcium-sensitive compound is detected as a measure of the voltage regulated calcium influx.

14. The method of claim 12, wherein the pharmacological agent that specifically reduces voltage regulated calcium influx mediated by a N-type calcium channel containing a $Ca_V2.2e[37a]$ subunit is an agent that reduces N-type calcium channel current densities in nociceptive neurons.

15. The method of claim 14, wherein the pharmacological agent that specifically reduces voltage regulated calcium influx mediated by a N-type calcium channel containing a $Ca_V2.2e[37a]$ subunit is useful as an analgesic agent.

16. A method for identifying compounds which selectively or preferentially bind a N-type calcium channel containing a $Ca_V2.2e[37a]$ subunit comprising,

providing a first cell or membrane encapsulated space which expresses a N-type calcium channel that contains a $Ca_V2.2e[37a]$ subunit,

providing a second cell or membrane encapsulated space which expresses a N-type calcium channel that does not contain a $Ca_V2.2e[37a]$ subunit, wherein the second cell or membrane encapsulated space is identical to the first cell except for the N-type calcium channel expressed,

contacting the first cell or membrane encapsulated space and the second cell or membrane encapsulated space with a compound, and

determining the binding of the compound to the first cell or membrane encapsulated space and the second cell or membrane encapsulated space,

wherein a compound which binds the first cell or membrane encapsulated space but does not bind the second cell or membrane encapsulated space is a compound which selectively binds the N-type calcium channel that contains a $Ca_V2.2e[37a]$ subunit, and wherein a compound which binds the first cell or membrane encapsulated space in an amount greater than the compound binds the second cell or membrane encapsulated space is a compound which preferentially binds the N-type calcium channel that contains a $Ca_V2.2e[37a]$ subunit.

17. The method of claim 16, wherein the N-type calcium channel that does not contain a $Ca_V2.2e[37a]$ subunit is a N-type calcium channel that contains a $Ca_V2.2e[37b]$ subunit.

18. A method for identifying compounds which selectively or preferentially bind to a $Ca_V2.2e[37a]$ isoform comprising,

providing a $Ca_V2.2e[37a]$ isoform polypeptide or nucleic acid,

providing a $Ca_V2.2e[37b]$ isoform polypeptide or nucleic acid,

contacting the $Ca_V2.2e[37a]$ isoform polypeptide or nucleic acid and the $Ca_V2.2e[37b]$ subunit isoform polypeptide or nucleic acid with a compound, and

determining the binding of the compound to the $Ca_V2.2e[37a]$ isoform polypeptide or nucleic acid and the $Ca_V2.2e[37b]$ isoform polypeptide or nucleic acid,

wherein a compound which binds the $Ca_V2.2e[37a]$ isoform polypeptide or nucleic acid but does not bind the human N-type calcium channel $Ca_V2.2e[37b]$ isoform polypeptide or nucleic acid is a compound which selectively binds the $Ca_V2.2e[37a]$ isoform, and wherein

a compound which binds the $Ca_V2.2e[37a]$ isoform polypeptide or nucleic acid in an amount greater than the compound binds the $Ca_V2.2e[37b]$ isoform polypeptide or nucleic acid is a compound which preferentially binds the $Ca_V2.2e[37a]$ isoform.

19. The method of any of claims 16-18, wherein the compound is an antibody or a antigen-binding fragment thereof.

20. The method of any of claims 16-18, wherein the compound is a nucleic acid molecule.

21. The method of any of claims 16-18, wherein the compound is a compound is a library of molecules.

22. The method of claim 21, wherein the library is a natural product library.

23. The method of claim 21, wherein the library is a library generated by combinatorial chemistry.

24. A method for preparing an analgesic agent, comprising

identifying an agent that selectively or preferentially reduces calcium channel current densities in nociceptive neurons mediated by N-type calcium channels containing a $Ca_V2.2e[37a]$ subunit, and

formulating the agent for administration to a subject in need of such treatment.

25. A method for preparing an analgesic agent, comprising

identifying a compound according to the method of any of claims 12-23, and

formulating the compound for administration to a subject in need of such treatment.

26. A double stranded RNA molecule specific for $Ca_V2.2e[37a]$ RNA.

27. The double stranded RNA molecule of claim 26, wherein the molecule is 21-23 nucleotides in length.

28. The double stranded RNA molecule of claim 26, wherein the molecule has a 3' overhang.

29. The double stranded RNA molecule of claim 28, wherein the 3' overhang is 2 nucleotides in length.

30. The double stranded RNA molecule of claim 26, wherein the molecule is a single molecule that comprises a hairpin structure.

31. A method for inhibiting calcium influx in a neuronal cell mediated by a N-type calcium channel containing a $Ca_V2.2e[37a]$ subunit comprising

contacting the neuronal cell with an amount of a $Ca_V2.2e[37a]$ inhibitor effective to inhibit calcium influx in the mammalian cell.

32. The method of claim 31, wherein the inhibitor is selected from the group consisting of an antibody which selectively binds the $Ca_V2.2e[37a]$ polypeptide, an antisense nucleic acid that reduces expression of a $Ca_V2.2e[37a]$ polypeptide, a siRNA that reduces expression of a $Ca_V2.2e[37a]$ polypeptide.

33. A method for treating a subject afflicted by pain mediated by a N-type calcium channel containing a $Ca_V2.2e[37a]$ subunit comprising

administering to a subject in need of such treatment an inhibitor of the $Ca_V2.2e[37a]$ polypeptide in an amount effective to inhibit voltage regulated calcium influx and thereby to reduce the pain.

34. The method of claim 33, wherein the inhibitor is selected from the group consisting of an antibody which selectively binds the $Ca_V2.2e[37a]$ polypeptide, an antisense nucleic acid that reduces expression of a $Ca_V2.2e[37a]$ polypeptide, a siRNA that reduces expression of a $Ca_V2.2e[37a]$ polypeptide.

35. The method of claim 33, wherein the inhibitor is administered prophylactically to a subject at risk of being afflicted with pain.

36. The method of claim 33, wherein the pain is neuropathic pain.